

U.S.S.N. 09/453,109
Filed: December 2, 1999

**AMENDMENT AND
RESPONSE TO OFFICE ACTION**

In the Specification

Please insert the following new heading and paragraph at page 1, line 7:

Statement Regarding Federally Sponsored Research

A1 This invention was made with government support under Contract Number BES-9813321 awarded by the U.S. National Science Foundation. The government has certain rights in the invention.

Please replace the paragraph beginning on page 8, line 24, with the following paragraph:

A2 In a preferred embodiment, the collection chamber is a standard or Luer-Lock syringe adapted to be connected to a microneedle array. See Figure 4 which illustrates a preferred embodiment wherein device 220 includes substrate 212 from which a three-dimensional array of microneedles 214 protrude. The device 220 also includes plunger 222 that is slidably secured to the upper surface of substrate 212 by plunger guide frame 224 using a restraint such as a Luer-lock interface 223. The substrate 212 can be attached or detached to a syringe 226 via a connector such as a Luer-lock type attachment 223. The plunger 222, guide frame (outer syringe housing) 224, and connector 223 connect to, form or contain reservoir 216. A Luer-lock type attachment alternatively may be used to secure the device to means, such as a pump, for controlling flow or transport through the device.

A3 Please replace the paragraph beginning on page 35, line 21, with the following paragraph:

Three-dimensional arrays of microtubes were fabricated from silicon, using deep reactive ion etching combined with a modified black silicon process in a conventional reactive ion etcher. The fabrication process is illustrated in Figures 8a-d. First, arrays of 40 μm diameter circular holes 132 were patterned through photoresist 134 into a 1 μm thick SiO_2 layer 136 on a two inch silicon wafer 138 (Figure 8a). The wafer 138 was then etched using deep reactive ion etching (DRIE) (Laermer, et al., "Bosch Deep Silicon Etching: Improving Uniformity and Etch Rate for

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Advanced MEMS Applications," *Micro Electro Mechanical Systems*, Orlando, Florida, USA (Jan. 17-21, 1999)) in an inductively coupled plasma (ICP) reactor to etch deep vertical holes 140. The deep silicon etch was stopped after the holes 140 reached approximately 200 μm deep into the silicon substrate 138 (Figure 8b). The photoresist 134 was removed, and a second photolithography step was used to pattern the remaining SiO₂ layer 136 into circles concentric to the holes, thus leaving ring shaped oxide masks 134 surrounding the holes (Figure 8c). The photoresist 134 was then removed and the wafer 138 was again deep silicon etched, while simultaneously the holes 140 were etched completely through the wafer 138 (inside the SiO₂ ring) and the silicon was etched around the SiO₂ ring 138 leaving a cylinder 142 (Figure 8d). The resulting tubes were 150 μm in height, with an outer diameter of 80 μm , an inner diameter of 40 μm , and a tube center-to-center spacing of 300 μm .

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Please replace the paragraph beginning on page 36, line 13, with the following paragraph:

Hollow metal microtubes were prepared without dry silicon etching, using a thick, photo-defined mold of epoxy. The sequences are illustrated in Figures 9a-e. First, a thick layer of SU-8 epoxy 144 was spin cast onto a silicon or glass substrate 146 that had been coated with 30 nm of titanium 148, the sacrificial layer. Arrays of cylindrical holes 149 were then photolithographically defined through an epoxy layer 144, typically 150 μm thick (Figure 9a). The sacrificial layer 148 at the bottom of the cylindrical holes 149 then was partially removed using a wet etching solution containing hydrofluoric acid and water (Figure 9b). A seed layer of Ti/Cu/Ti (30 nm/200 nm/30 nm) 139 was then conformally DC sputter-deposited onto the upper surface of the epoxy mold and onto the sidewalls of the cylindrical holes 149 (Figure 9c). As shown in Figure 9c, the seed layer 139 was electrically isolated from the substrate 146. Subsequently, NiFe 145 was electroplated onto the seed layer 139 (Figure 9d), and the epoxy 144, the substrate 146, and the sacrificial layer 148 were removed, leaving the electroplated structure (microtubes) consisting of the Ti/Cu/Ti seed layer 139 and the NiFe layer 145 (Figure 9e). The resulting microtubes are 200 μm in height with an outer diameter of 80 μm , an inner

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diameter of 60 μm , and a tube center-to-center spacing of 150 μm . The holes in the interior of the microtubes extend through the base metal supporting the tubes.

Please replace the paragraph beginning on page 37, line 18, with the following paragraph

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Then, the upper surface of the epoxy 52 was etched away using an O₂/CHF₃ plasma until approximately 1 to 2 μm of the needle tips 51 were exposed, protruding from the epoxy 52 (Figure 10b). The silicon was then selectively removed by using a SF₆ plasma (Figure 10c). The remaining epoxy mold 52 provided a negative of the microneedles with a small diameter hole where the tip of the silicon needle protruded. After the removal of the silicon, a seed layer of Ti-Cu-Ti 54 was conformally sputter-deposited onto the top and sidewalls of the epoxy micromold 52. Following the same process sequence as described in Example 5, NiFe 55 was then electroplated onto the seed layer 54. Finally, the epoxy 52 was removed using an O₂/CHF₃ plasma, leaving a released structure of hollow metal microneedles 56 formed of NiFe 55 layer and Ti-Cu-Ti 54 seed layer (Figure 10d). The microneedles were made in a 20 x 20 array, and were 150 μm in height with a base diameter of 80 μm , a tip diameter of 10 μm , and a needle-to-needle spacing of 150 μm .